PHASE II TRIAL OF CG8123, AN AUTOLOGOUS CANCER VACCINE (GVAX), IN PATIENTS WITH SELECTED STAGE IIIB AND IV BRONCHIOLOALVEOLAR CARCINOMA (BAC)

Nontechnical Abstract

Bronchioloalveolar carcinoma (BAC) is a kind of non-small cell lung cancer (NSCLC) that is increasing in incidence. BAC usually appears confined to the lung spreading along the small airways. BAC represents about 2 - 5% of new NSCLC cases and is reported to be more common in females, non-smokers, and younger patients compared to other kinds of NSCLC. Patients with advanced BAC are more likely to have BAC in both lungs, but less likely to have it spread into other organs. Among patients with Stage IIIB and IV NSCLC, a median survival of 15 months in BAC compares favorably to the median survival of 10 months seen in other kinds of NSCLC.

Few clinical trials have been done in BAC patients and it is unclear whether chemotherapy has equal effect in BAC compared to other kinds of NSCLC. The only prospective Phase II BAC trial was recently completed by the Southwest Oncology Group (**S9714**). Fifty-eight Stage IIIB and IV BAC patients were treated with paclitaxel 35 mg/m^2/24 hours by 96-hour infusion on a 21-day cycle (140 mg/m^2 total per cycle). The median survival was twelve months and the three-year survival was 10%. The toxicity of 96-hour paclitaxel was considerable. Although localized BAC can be cured with surgery, at the present time, effective treatment for advanced BAC remains unclear.

There is clearly a need to develop other ways to treat advanced BAC. p53 gene transfer using a virus system is being explored at the University of Wisconsin. CG8123 (formally known as GVAX), an anti-tumor vaccine developed using the patient's own tumor cells, has also demonstrated activity in BAC. Because the vaccine is developed using the patient's own tumor cells, tumor tissue is required from each patient - to manufacture their individual vaccine. This usually requires a surgical procedure to remove an adequate amount of tissue. In a Phase I study of CG8123 in NSCLC, two of three BAC patients treated with CG8123 had durable complete responses lasting 9 and 16 months respectively. As a result of these findings, we are proposing that CG8123 be studied in a Phase II study in BAC. Vaccines have not been specifically studied in BAC prior to this trial.

Stage IIIB/IV BAC patients with available tumor to harvest for vaccine processing will be enrolled. About 58 patients who have not received other treatments for BAC will take part in this study. Another 41 patients who have received prior treatments for BAC will participate. Allowing for a percentage of vaccine production failure of 25%, about 44 previously untreated and 31 previously treated patients will be eligible for analysis.

In the planned study, patients will have surgery to get tumor for production of the vaccine. CG8123 will be manufactured at a central facility. All patients with successful manufacture of enough vaccine will receive five vaccine treatments – given two weeks apart. All patients will be followed for a maximum of three years.

The success of the study will be measured by looking at several endpoints including the success of the vaccine manufacture, the safety of the vaccine and quality of life. Measurements of the vaccine's activity will include overall survival, time until tumor growth, tumor shrinkage and immunologic response.